REMARKS

Applicants respectfully request entry of the Amendment and Response.

Claims 50, 51, 53, 63 and 65-66 have been amended to further clarify the claimed invention. Applicants submit the Amendment is supported by the specification, including for example at page 9, lines 5-17, page 19, line 25 to page 20, line 6, page 39, line 31 to page 40, line 5, page 42, lines 4-6, 48, lines 25-28, page 49, line 14 to page 50, line 13, and raise no issues of new matter.

Claim 67 is new and is supported throughout the specification including at page 39, lines 26-28; page 43 lines1-11; page 43, lines 20-23; and page 48, lines 25-28.

Claims 52, 54-62 and 64 have been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

Elections/Restrictions

Applicants acknowledge that the species election with respect to claim 53 has been withdrawn. As indicated by the Examiner, the non-elected species have been rejoined and examined on the merits.

Oath/Declaration

The Office Action alleges the claims contain new matter not present in the parent application. The Office Action therefore alleges that a new oath or declaration in compliance with 37 CFR 1.67(a) is required. Applicants respectfully traverse this objection. The claims as amended do not contain new matter for the reasons discussed below. Withdrawal of this objection is respectfully requested.

Priority

The Office Action alleges the priority claim is incorrect in view of the new matter rejection. Applicants respectfully traverse this objection. The claims as amended do not contain new matter for the reasons discussed below. Withdrawal of this objection is respectfully requested.

Specification

The Office Action alleges the specification does not comply with the requirements of 37 C.F.R. § 1.821 through § 1.825 for reasons set forth in an attached Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence Disclosures. The specification has been amended to include sequence identifiers. Applicants note that a Request to Transfer Previously Filed Sequence Information was filed on November 25, 2003 with a paper copy of the sequence listing. The specification has been amended to direct its entry into the specification.

New Matter

Claims 51-53 and 62-64 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. This is a new matter rejection. Claims 52 and 62 have been cancelled rendering the rejection of this claim moot. Applicants respectfully traverse this rejection with respect to the remainder of the claims.

The Office Action indicated methods of identifying a candidate agent that inhibits CHAG gene expression in isolated cells was supported by the specification. The claims as amended recite a method of identifying an inhibitor of CHAG gene expression in isolated cells. The Office Action alleges the specification does not disclose using a CHAG polynucleotide comprising SEQ ID NO:9 with a candidate agent (antisense nucleic acid) to identify if the agent inhibits CHAG expression in a genus of cells. Applicants respectfully do not agree.

Applicants understand that the Examiner contends that the instant application adds and claims additional disclosure not present in the prior application. Applicants have reviewed the parent application and do not find any additional disclosure. Due to differences in formatting and line spacing, the page numbering and line numbering in the present application and the 09/554,169 application (hereinafter the '169 application) do not correspond. Applicants further submit that all of the prior filed applications support the currently pending claims.

The written description requirement requires that Applicants' specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir.

1991). As noted in the Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) Fed Reg. 1099, 1105 (2001); see also, In re Wertheim, 191 USPQ 90,97 (CCPA 1976). The guidelines further state that "[(The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." 66(4) Fed. Reg. at 1107; 191 USPQ at 97, (emphasis added). Compliance with the written description requirement does not require an applicant to describe exactly the subject matter claimed; rather, the description must clearly allow a person of ordinary skill in the art to recognize that he or she invented what is claimed. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The test is whether the originally filed specification reasonably conveys to a person having ordinary skill in the art that applicant had possession of the subject matter later claimed. In re Kaslow, 217 USPQ 1089 (Fed. Cir. 1991).

Applicants submit the claims as amended do not introduce new matter. Applicants provide the structure of the sequence (*e.g.* SEQ ID NO:9) and the sequence provides the structure of any effective antisense molecules such that one of skill in the art would be able to immediately envisage members of the genus embraced by the claim. Applicants note the written description guidelines provide that disclosure of a nucleic acid sequence provides for written description for antisense molecules. See written description guidelines at page 56 (copy attached).

The examiner suggests that Applicants are picking and choosing in the specification to find support for the claimed subject matter. However, that this is not the standard for written description but rather whether the specification reasonable conveys to one of skill in the art that applicants were is possession of the claimed subject matter. It is clear that the specification describes methods of identifying antagonists (inhibitors) of CHAG proteins and nucleic acids. See, for example, page 46 lines 18 to page 47 line 2 and page 48, lines 11-17. Applicants disclose that CHAG antisense nucleic acids can be inhibitors of CHAG expression or activity, and that CHAG antisense molecules can be assayed for the ability to modulate expression and/or activity of CHAG. See, for example, the specification at page 39, lines 26-28; page 43 lines1-

11; page 43, lines 20-23; page 48, lines 25-28 and the '169 application at page 40, lines 20-22. Applicants disclose that molecules that inhibit CHAG, such as CHAG antisense nucleic acids, can be used to treat or prevent cardiac hypertrophy. See, for example, the specification at page 32, lines 16-20 and the '169 application at page 27, lines 16-20. Applicants disclose that a therapeutic of the invention can be assayed for activity in treating or preventing hypertrophy in a cellular assay. Isolated cells exhibiting an indicator of cardiac hypertrophy are contacted with a candidate therapeutic agent and assayed for a change in the level of indicator. See, for example, the specification at page 50, lines 4-10 and the '169 application at page 41, lines 22-27. Expression of CHAG is an indicator of caridac hypertrophy. See for example, the working examples beginning at page 58 of the specification and the '169 application beginning at page 48. CHAG antisense nucleic acids are specifically recited, for example, at page 39, lines 26-28 (page 33, lines 12-14 of the '169 application) as a therapeutic for treating or preventing cardiac hypertrophy. Methods for detecting expression of CHAG polynucleotides in a cell are described in the specification, for example, at page 49, lines 14-26 (page 41, lines 4-14 of the '169 application).

In view of the forgoing, Applicants submit the specification provides support for the claimed subject matter and does not represent new matter. Withdrawal of the new matter rejection is respectfully requested.

Written Description

Claims 50, 51, and 63-66 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Claim 64 has been cancelled rendering the rejection of this claim moot. Applicants respectfully traverse this rejection with respect to the remainder of the claims.

The Office Action alleges the genus of molecules recited in claims 50 and 51 are not recited in a specific biochemical or molecular structure and that the mere contemplation of the claimed genus in the specification is not sufficient to support the presently claimed invention directed to a genus of molecules that specifically bind to a nucleic acid encoding CH-9 or a protein encoded by a CH-9 nucleic acid. Therefore, the Office Action alleges that one of skill in

the art could not envision the genus of claimed molecules or agents. Applicants respectfully do not agree.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. MPEP § 2163(I) (emphasis added). The claims as amended recite methods of identifying molecules or agents that bind a novel ligand. The ligand can be a protein having at least 95% identity to an amino acid sequence encoded by SEQ ID NO:9, a fragment of the protein comprising a domain of the protein, or a polynucleotide encoding a protein having at least 95% identity to an amino acid sequence encoded by SEQ ID NO:9. The method, not a genus of molecules that can be screened by the method, is the claimed invention. Applicants submit the written description requirement does not require the specification to describe the biochemical or molecular structure of the genus of molecules or how to make the genus of molecules. Any molecule can be screened for binding to the ligand.

As discussed above, the specification provides sufficient support. One skilled in the art reading the specification would reasonably conclude that Applicants had possession of the claimed methods. Withdrawal of the rejection is respectfully requested.

Enablement

Claims 50-53 and 62-64 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Claims 52, 62 and 64 have been cancelled rendering the rejection of these claims moot. Applicants respectfully traverse this rejection with respect to the remainder of the claims.

There are many factors to be considered in an enablement analysis, including the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation. *MPEP* 2164.01(a) citing *In Re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The specification must enable the claimed subject matter without undue experimentation. The test for undue experimentation "is not merely quantitative, since a considerable amount of experimentation is possible, if it is merely routine, or the specification in question provides a reasonable amount of guidance with respect to the

direction in which the experimentation should proceed." *MPEP 2164.06.* Indeed, "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." *MPEP 2164.01.*

The Office Action alleges the specification does not provide sufficient guidance to use the methods in a cell in vivo. The Office Action acknowledges the specification provides sufficient guidance for use of the method in an isolated cell. Without acquiescing to the rejection and solely for the purpose of advancing prosecution, claim 51 has been amended to recite contacting an isolated cell with an antisense nucleic acid. Claim 50 has been amended to recite contacting the ligand in vitro with the molecule.

The Office Action alleges the specification does not provide sufficient guidance to use the methods outside of a cell. Applicants respectfully do not agree.

Claim 51 as amended recites contacting an isolated cell comprising a CHAG polynucleotide. Therefore, the rejection is discussed insofar as it applies to claim 50. Claim 50 is drawn to a method of identifying a molecule that binds to a ligand. The specification describes binding assays that do not require a cell. For example, the ligand can be a member of a library immobilized on a solid surface (page 47, line 3 to page 48, line 18). Cell-free assays for detecting the binding of a molecule to a ligand were conventional and known. Therefore, one of skill in the art would have reasonably concluded that claimed method does not require a cell.

In view of the guidance provided in the specification and the skill in the art, Applicants submit one of skill in the art could practice the full scope of the claimed methods without undue experimentation. Withdrawal of the rejection is respectfully requested.

Indefinite

Claims 50-53 and 62-63 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 52 and 62 have been cancelled rendering the rejection of these claims moot. Applicants respectfully traverse this rejection with respect to the remainder of the claims.

The Office Action alleges claims 50 and 51 omit the essential step of identifying where the contacting step is taking place. While not acquiescing to the rejection and solely to expedite

prosecution, claim 51 as amended recites contacting an isolated cell comprising a CHAG polynucleotide, and claim 50 as amended recites contacting the ligand in vitro. An omitted step is only considered essential if the omitted step is described in the specification as necessary to practice the claimed invention. MPEP § 2172.01. With respect to claim 50 or 51, the specification does not require the contacting step to take place in a test tube, microtiter plate, cell, etc., and the Office Action has failed to provide any evidence from the specification indicating that the omitted step is necessary to practice the claimed invention. Applicants therefore submit the currently pending claims are not indefinite.

Withdrawal of the rejection is respectfully requested.

Summary

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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PATENT TRADEMARK OFFICE

Example 15: Antisense

Specification: The specification discloses a messenger RNA sequence, SEQ ID NO: 1, which encodes human growth hormone. The specification states that the invention includes antisense molecules that inhibit the production of human growth hormone. The specification describes an art-recognized method of screening for antisense molecules that is called "gene walking." Gene walking is said to involve obtaining antisense oligonucleotides that are complementary to the target sequence.

Claim:

An antisense oligonucleotide complementary to a messenger RNA having SEQ ID NO: 1 and encoding human growth hormone, wherein said oligonucleotide inhibits the production of human growth hormone.

Analysis:

A review of the full content of the specification indicates that the complement of SEQ ID NO: 1 is essential to the operation of the claimed invention. The general knowledge in the art is that any full-length complement of a target mRNA inhibits the function of the mRNA and is therefore an antisense oligonucleotide. Thus, one of skill in the art would view applicant's disclosure of a coding sequence, with the statement that the invention includes antisense oligonucleotides, as an implicit disclosure that the full-length complement of SEQ ID NO: 1 is an antisense oligonucleotide.

It is generally accepted in the art that oligonucleotides complementary to a messenger RNA, including fragments of the full-length complement, have antisense activity when they match accessible regions on the target mRNA. Generally, the closer the complementary fragment is to full length, the greater the likelihood it will have antisense activity. In addition, oligos that retain complementarity to the Shine-Delgarno sequence usually have antisense activity.

The claim is drawn to the genus of antisense molecules that inhibit the production of human growth hormone encoded by SEQ ID NO: 1. There is a single species described with a complete structure, i.e., the full-length complement of SEQ ID NO: 1. In addition to the full-length complement, the genus includes fragments of the complement that retain antisense activity.

The procedures for making oligonucleotide fragments of the SEQ ID NO: 1 complement are conventional, e.g., any specified fragment can be ordered from a commercial synthesizing service. The procedures for screening for antisense activity are also conventional, and the specification describes the assay needed to do gene walking. The experience accumulated in the art with gene walking is that numerous regions of a target are accessible, that these regions are identified routinely, and that antisense oligonucleotides are complementary to these accessible regions. The full-length complement and longer fragments match multiple accessible regions; shorter fragments match fewer accessible regions.

When considering the distinguishing characteristics of the claimed invention, the sequence provided in the specification defines and limits the

structure of any effective antisense molecules. The specification also teaches the functional characteristics of the claimed invention as well as a routine art recognized method of making and screening for the claimed invention. Considering the specification's disclosure of:

(1) the sequence (SEQ ID NO: 1) which defines and limits the structure of any effective antisense molecules such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim, and

(2) the functional characteristics of the claimed invention as well as a routine art-recognized method of screening for antisense molecules which provide further distinguishing characteristics of the claimed invention, along with

(3) the general level of knowledge and skill in the art,

one skilled in the art would conclude that applicant was in possession of the invention.

Conclusion: The claimed invention is adequately described.